THE SYMPTOMATOLOGY OF TUMOURS INVOLVING THE HYPOPHYSIS CEREBRI.

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It is generally recognized that tumors of or involving the pituitary body may in addition to the results arising from local or general cerebral pressure induce symptoms directly due to destruction or interference of the function of this structure. It is generally admitted that the hypophysis is either enlarged or diseased in every case of acromegaly.

What relation the changes in the pituitary body bear to the acromegalic symptoms is however still a matter of speculation ? A number of cases of tumours involving the destruction of the hypophysis have been reported, chiefly by Weir Mitchell, Drs. Anders and Cattell, and Guy Hinsdale, where no symptoms of acromegaly where present.

This paper is chiefly a record of two cases of a similar character, in neither of which were there any symptoms of acromegaly. In one case the symptoms in addition to the direct cerebral pressure signs resembled a mixture of myxœdema and pernicious anæmia, while in the other the symptoms were those of a somewhat rapid infiltrating neoplasm of the anterior part of the base of the brain.

CASE I.

Perithelial Angio-Sarcoma of the Pituitary Body—Symptoms—headache, vomiting and temporal hemianopia—Finally infiltration of the growth into the ethmoid and spheroidal cells causing hæmorrhage from the nares—No symptoms of acromegaly or other forms of nutritional disturbance.

Miss K., aged 35, a miniature painter, was admitted on the 2nd December '98, complaining of headache, dimness of vision, and occasional vomiting . She says that the headache and dimness of vision have been troublesome for upwards of eighteen months. The failure of vision was noticed first in the left eye and she observed that the pupil of this eye was larger than the right. Three months previous to admission the sight of the right eye was found to be also failing, and the pupil of that eye to be becoming larger. The vomiting which occurs about every month, lasting from one to three days, was first noticed on March of 1898.

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She was born in Eastern Ontario, and always lived there, except for a period of 6 years, when she resided in the state of Illinois. With the exception of measles and whooping-cough there is no history of any illness. She has four brothers and five sisters living, all in good health. One brother died from pulmonary tuberculosis, and a sister from heart trouble, She was much worried for months previous to the onset of headache and dimness of vision, and had been treated for nervous prostration.

Present Condition. She is a tall and well nourished woman, 35 years of age. She is able to walk about but prefers lying in bed on her back, as in this position she suffers less from headaches. She is more than ordinarily intelligent, her mental state on admission being as far as she herself or others could judge, fully normal.

Headache. Pain in the head is her great complaint. It is referred chiefly to (1) the left temporal and parietal regions; in the left eyeball and over the left brow; (2) to the occiput, just below the occipital protuberance, shooting downwards and often forwards, on both sides often entirely circling the neck.

The pain she says is continuous but it is frequently intensified especially on movement, on percussion and at times spontaneously.

Dimness of vision. Three months before her admission into the hospital, Dr. Stirling had an opportunity of examining her eyes and found the following condition present.

Right Eye. 5-9, outer half of the field gone, light perception reduced 5°; the pupil active to light and accommodation but indirect action from left eye lost.

Left Eye. Light perception reduced 8°. She is able to count fingers at 2 feet in the lower and outer part of the field but nowhere else Pupil is 7 mm. in diameter, immobile to light and accommodation. There was a slight non paralytic divergence.

There was simple atrophy of both optic nerves, without any diminution in the size of the large vessels.

Three months afterwards, Dr. Buller found a more advanced condition of atrophy there being just perception of light in the left eye, and a marked diminution now all over the right field. He also reported a state of simple atrophy without diminution of the large vessels. The diminution of light perception in the right eye was so marked that he was not able to map out the field.

Her voluntary power is not in any way impaired. Nutrition is good. The knee jerks are much diminished, while the superficial and organic reflexes are normal. There is no disturbance of any form of the muscular sense. The general sensibility is not in any degree impaired and with the exception of the disturbance in the functions of the optic nerves already referred to the special sense nerves are normal.

Menstruation began when she was thirteen years of age and continued one year when it permanently ceased.

The urine had a sp. gr. of 1025 contained ½ per cent. of albumen together with numerous granular and hyaline casts.

The subsequent course was characterised by more or less continuous and severe headache, by occasional vomiting, and gradually increasing stupor. A few days previous to her death on the 7th Jan. '99 there was a discharge of a bloody fluid from both the anterior and posterior nares. The immediate cause of death was hyperpyrexia.

I am indebted to Dr. A. G. Nicholls, assistant pathologist to the Royal Victoria Hospital for the following account of the post mortem.

In addition to the morbid changes met with the brain, the following were found:

There was a subacute diffuse nephritis in both kidneys. The uterus infantile in type, being only 5.25 c.m. long. The ovaries were small, fusiform in shape and without noticeable scarring, and slightly fibroid.

The Brain. The calvarium was normal. The dura was thin showing the convolutions of the brain through its substance. It was congested and exuded blood. The convolutions were flattened on both sides, chiefly over the vertex and posteriorly. The frontal convolutions appeared to be normal. There was considerable exudation of clear fluid about the base of the brain.

On removing the brain a tumour mass was found at the base, lying in the sella turcica, and occupying the site of the pituitary gland, of which no vestige could be seen. The tumour measured 5 cm. long by 4.75 cm. broad. The upper surface was lobulated, forming grape-like masses of a reddish translucent colour, of soft consistence, and hæmorrhagic appearance. There were two large lateral lobes with 3 smaller ones anteriorly. The under surface of the tumour was very soft and diffluent, of the appearance of raspberry-jelly. This was probably due to manipulation. The tumour lay in the median line with a tendency to the left side. There was an oval excavation on the base of the brain in which the mass rested. The sella turcica was greatly enlarged in all directions corresponding to the main mass of the tumour below. The body of the sphenoid was eroded from pressure, the bone being as thin as paper. The sphenoidal and ethmoidal cells contained a jelly-like mass similar to the tumour. The posterior nares contained blood-stained mucus. On the left side in front the tumour passed beneath the dura of the cranial base reaching along the lesser wing of the sphenoid as far as the back of the left orbit. It had not, however, invaded the orbit. The growth had reached the top of the pharynx without causing any perceptible bulging. The tumour pressed directly upon the optic commissure which was flattened. It reached backward to a point 2 cm.

anteriorly to the pons, compressing the left crus. Other cranial nerves seemed not to be directly involved.

The specimen was hardened in bulk in formol—Müller.

At closer inspection the mass was found to be bounded, at least above, by a thin fibrous membrane, presumably the pia mater. Several sections were made through its substance, and through the optic chiasm, pons, medulla, left crus and cord.

Microscopically, the tumour was found to be enclosed in the upper surface by a laminated fibrous tissue membrane, presumably the pia mater. The finer structure of the mass varied somewhat in different parts. In the main it consisted of delicate capillary blood-vessels with elongated cells having oat-shaped nuclei. The blood-vessels were composed of basement membranes lined with flat endothelial cells; they were for the most part small but in a few instances formed actual cavernous sinuses. The elongated cells were arranged about the blood-vessels, their long axes being placed radially to the centre of the vessel. This gave the tumour the appearance of being formed of a series of rings. In other places the elongated cells formed long finger-like processes running in various directions and without the same definite relationship to the vessels. On the under surface of the tumour small spicules of bone were seen showing that the new growth had forced its way through the body of the sphenoid. At the margin of the growth two or three very cellular nodules were seen which had a close resemblance to round-celled sarcoma. On the whole as the tumour was composed largely of short spindle cells it had the appearance of a sarcoma, and owing to the relationship to the vessels it must have started from the perithelium. No remains of the pituitary body were seen, nor was colloid present,

Diagnosis. Perithelial angio-sarcoma of the pituitary body.

Sections through the optic chiasm showed that the optic nerves were in a state of extensive degeneration, the myelin sheaths being broken up and reduced to globular masses. The blood-vessels were distended and surrounding them were masses of small round cells.

Sections through the pons, medulla, left crus, and cord, showed nothing abnormal.

The symptoms in this case extended over a period of about twenty months, and were clearly indicative of a cerebral growth in the neighborhood of the optic chiasm. There were no symptoms whatever of acromegaly, myxœdema or pernicious anæmia. I would like, however, to call attention to two changes which have been frequently met in cases of tumours involving the pituitary body.

These are cirrhotic changes in the kidneys, uterus and ovaries. Boyce in his valuable paper on hypophysial growths gives details of at least four cases where the kidneys were found to be granular.

CASE II.

Endothelioma of the base of the brain—Causing pressure on the chiasma and obliterating the pituitary body—Symptoms of a cerebral growth extending over 9 years—Right temporal hemianopia—Profound anæmia—A general appearance not unlike that seen in myxœdema—No changes in the bony tissue.

Mr. W—, a merchant, aged 42, came first under the observation of Dr. Stirling in Feb. 1888, complaining of failing vision, headache and previously and this was I believe the first evidence of any intra-cranial trouble.

He had been for a number of years and up to the time of the appearance of his present complaints a heavy drinker. There was no history or evidence of tuberculosis or syphilis. He complained of a dull frontal headache but neither at this period or any time during the prolonged course of his illness, was headache a prominent symptom. In walking he more or less constantly had what he called a giddy sensation with a tendency to fall forwards. Vomiting of a cerebral character was present for some months during the early period of the disease. Dr. Stirling's examination of the eyes revealed the following changes:

Left Eye. There is no perception of light. The pupil is semidilated and immobile, but reacts on stimulating the right eye with light.

Right Eye. Complete blindness to the outer side of the field. The inner side was amblyopic, vision being reduced to counting fingers at twelve feet. In reading type he is able to pick out a letter of the largest size (No. 16) here and there. In this area the perception of green was found to be very defective, and after looking at green for sometime there was an after image in pink.

Examination of the fundus revealed in the left eye white atrophy of the disc with somewhat contracted vessels. In the right eye the disc was simply pale.

There was no objective disturbance of either sensation or motion. He complained however of numbness in the hands. He had frequent flushings followed by profuse perspirations about the head and neck. The knee jerks were slightly exaggerated but the superficial and organic reflexes were normal.

The further course of this case was very slow, six years elapsing before his death in 1894. His sight entirely failed in August 1889. He became very fat and anæmic. The face and extremities were puffy, but in no part was there pitting on pressure. The puffy, pale skin presented a very striking clinical picture. The pallor of the skin was noticed when he first came under observation in 1888, but it steadily increased. In 1892, he presented the typical appearance of a person suffering from pernicious anæmia, the skin having a typical lemon-yellow tint, while the general state of nutrition appeared to be unusually good. In March 1893 Dr. Gunn examined the blood. He found 2,800,000 red cells and the proportion of white to red as 1 to 1500. The red cells were irregular in size, microcytes being abundant, no nucleated red cells were found. Four months later a second examination of the blood was made by Dr. Gunn. He found 2,100,000 red cells, and the proportion of white to red as 1 to 1600. The urine was free from both albumen and sugar.

The anæmia remained up to death but did not present any changes different from the last above recorded examination. His appetite remained good and was even at times voracious. He was annoyed with photopsiæ, and during the last two years of his life he complained more or less constantly of hallucinations of vision, smell, taste and hearing and of general sensibility. He often imagined that burglars were breaking into the house, maintaining that he not only heard but saw them. He kept a revolver under his pillow to punish any burglar that would attempt to come near him.

He frequently made mention of what he called "beasties" crawling over his skin and would stoutly maintain that he not only felt but saw them. This was when he had no perception of light in either eye. Although his general nutrition and strength were fair he spent almost the whole of his last year in bed. When urged to get up, he would make answer that he would do so the following day.

Summary of the symptoms and course :

1. Gradual loss of vision in both eyes, going on to total blindness in the left and temporal hemianopia in the right followed later on by total extinction of the perception of light.
2. There was complaint in the earlier months of his illness of frontal headache and of occasional vomiting.
3. The presence of more or less constant giddiness throughout the course of his disease with a tendency at first to fall forwards and afterwards to one side.
4. Profuse intermittent flushings and perspirations about the face and neck, but the skin of other parts was dry and harsh.
5. Slow cerebration, as evidenced by a slow drawing speech and slowness in answering questions. There was also great apathy and drowsiness and lowered .temperature.
6. Hallucinations of sight, smell, hearing and of general sensibility.
7. A very pronounced lemon tint of the skin, resembling in this respect the appearances considered to be characteristic of pernicious anæmia. The blood changes corresponded also to those met with in pernicious anæmia.

8. Œdematous-like condition of the hands and feet, but no pitting on pressure.
9. During the last two years of his life, he kept his bed more or less constantly, taking little or no interest in anything but still able to talk and answers questions intelligently. He finally died in a state of coma.

Diagnosis. The general symptoms, headache, vomiting, vertigo and optic atrophy pointed clearly to a cerebral tumour, while the temporal hemianopia localized this to the optic chiasm. Had the visual disturbance been seen earlier it is highly probable the limitation of the field would have been met in both eyes. The absence of the pupillary reflex indicated that the lesion must have been situated between the left eye and the basal optic nuclei. Further, the optic atrophy showed that the lesion could not be further back than the basal nuclei, as in lesions of the optic radiations or cortex, white or essential atrophy is exceedingly rarely if ever visible at the optic disc. The slow growth of the tumour would account for the absence of the choked disc, time being sufficient to allow of the formation of lateral drainage or gradual distention of the sheath

When the patient was first examined the obtunding of the nasal half of the light field, together with the defective perception of green, pointed to interference with the conduction of the remaining active portion of this nerve. There was a concentric and a fairly equal contraction of the field for white and colours pointing to a slow growth.

Prof. Adami, who performed the post mortem examination found a large cancerous tumour of the pituitary. The bone in the neighborhood was found greatly atrophied and the fossa greatly enlarged.

The growth was not perfectly symmetrical, it extended more to the left than the right side. The right olfactory was pushed to one side, while the growth infiltrated anteriorly above the left olfactory nerve. The thyroid gland was found to be normal.

The portion of the tumour examined was enclosed in a laminated fibrous tissue capsule,—the pia mater. The tumour was composed of rounded or oval masses of cells surrounded by loose connective tissue, the whole at first sight suggesting carcinoma simplex. On examining more closely however, it was seen that the cells did not conform to the carcinoma type. The walls of connective tissue which enclosed the cellular masses were lined with elongated and flattened cells, fusiform when viewed edgeways. At other places when the section was more oblique, these cells could be seen to be irregularly diamond-shaped with large clear oval nuclei—typical endothelial cells. The cells forming the cell-masses were various in shape, being generally elongated with bluntly oval nuclei, others however being irregular in outline with a more rounded nucleus. They had in places a curious tendency to form small whorls, and in such cases the component cells were considerably flattened. The tumour was not specially vascular, nor did it show any tendency to degeneration. No pituitary structure was seen.

Diagnosis. Endothelioma.

The general symptoms of an intracranial growth, as headache, vomiting, vertigo, optic atrophy, were sufficiently pronounced to allow such a diagnosis and the locality of the growth was clearly indicated by the temporal hemianopia. An especial interest arises in connection with an explanation of the peculiar combination of symptoms, viz: a myxœdematous-like state and the pallor of the skin. How are these conditions to be explained ? Have they any connection with the destruction of the pituitary body ?

In a recent paper by Pechkranz of Warsaw (*Necrolog. Centblt. vol. 18, page 254*) on a case of sarcoma of the pituitary body, particular mention is made of a myxœdematous-like appearance that was a prominent feature. The author considers it identical with the pachyacria mollis ([illegible]ld, a state in which the dystrophy is confined to the soft tissues [illegible] distinction to acromegaly to which he applies the term pachya[illegible]ea. In Pechkranz's case the bony tissues were found normal.

In a few cases of myxœdema changes have been met with in the pituitary body and instances are on record where both diseases have existed together. Dr. Anders *(in Nervous and Mental Diseases, Jan. 1892)* reports a case of hæmorrhagic tumour of the pituitary body and infundibulum in a case of pernicious anæmia in a female, aged 34. The symptoms which developed after typhoid fever were giddiness, headache, nausea, slight loss of consciousness and delirium. I simply place this second case on record without the addition of any hypothesis as to a possible causal connection between the pituitary growth, the anæmia and myxœdematous-like state.